



Translation

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 663477	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2002/010816	International filing date (day/month/year) 18 October 2002 (18.10.2002)	Priority date (day/month/year)
International Patent Classification (IPC) or national classification and IPC C12N 15/09, 15/12, C07K 14/47, C12Q 1/37, G01N 33/53, 33/573, 33/58, 33/68, 33/96		
Applicant JAPAN AS REPRESENTED BY THE PRESIDENT OF NATIONAL CARDIOVASCULAR CENTER		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.	
2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.	
3. This report is also accompanied by ANNEXES, comprising:	
a. <input type="checkbox"/>	(sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
<input type="checkbox"/>	_____ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
<input type="checkbox"/>	_____ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
b. <input checked="" type="checkbox"/>	(sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) <u>1</u> , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:	
<input checked="" type="checkbox"/> Box No. I	Basis of the report
<input type="checkbox"/> Box No. II	Priority
<input type="checkbox"/> Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/> Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/> Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/> Box No. VI	Certain documents cited
<input type="checkbox"/> Box No. VII	Certain defects in the international application
<input type="checkbox"/> Box No. VIII	Certain observations on the international application

Date of submission of the demand 12 March 2004 (12.03.2004)	Date of completion of this report 30 June 2004 (30.06.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International Application No.

PCT/JP2002/010816

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

- ☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	2-6, 10-14, 16-19	YES
	Claims	1, 7-9, 15	NO
Inventive step (IS)	Claims	5-6	YES
	Claims	1-4, 7-19	NO
Industrial applicability (IA)	Claims	1-19	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Blood, August 2002, Vol. 100, No. 3, pages 778-785

Document 2: EMBO J., 1986, Vol. 5, No. 8, pages 1839-1847

Document 3: Blood, 1998, Vol. 91, No. 6, pages 2032-2044

Claims 1, 7-9 and 15

The subject matters of claims 1, 7-9 and 15 do not appear to be novel in view of document 1 cited in the ISR.

Document 1 describes a polypeptide consisting of A1-A2-A3 domain of human VWF. The document also describes that if the said polypeptide is kept in contact with blood plasma, the activity of ADAMTS13 can be tested. Though the document does not state the particular amino acid sequence of the said polypeptide, it is considered to correspond to a sequence from the 1242nd to 1875th of SEQ ID NO:1, considering document 2.

Therefore, the subject matters of claims 1, 7-9 and 15 cannot be substantially distinguished from the invention described in document 1.

Claims 7 and 8

The subject matters of claims 7 and 8 do not appear to be novel in view of document 2 cited in the ISR.

Document 2 describes human VWF and also discloses its amino acid sequence (corresponding to SEQ ID NO:1 of the present application). Since the said amino acid sequence is considered to be at least 70% homologous to the amino acid sequence of the polypeptide described in any one of claims 1-6, the subject matters of claims 7 and 8 cannot be substantially distinguished from the invention described in document 2.

Claims 10-14

The subject matters of claims 10-14 do not appear to involve an inventive step in view of document 1 cited in the ISR.

For example, introducing one or several mutants into a polypeptide and further binding a tag sequence are techniques well-known to a person skilled in the art, and could have been carried out as required.

Furthermore, employing the constitution of the subject matters of claims 10-14 is not considered to exhibit any especially remarkable effect.

Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:
- a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

** If item 4 in Box No. 1 applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V

Claims 16-19

The subject matters of claims 16-19 do not appear to involve an inventive step in view of document 1 cited in the ISR.

A person skilled in the art could have, as required, for example, (1) turned the method of measuring the activity of ADAMTS13 into a high-throughput one and (2) used the method for diagnosis.

Furthermore, employing the constitution of the subject matters of claims 16-19 is not considered to exhibit any especially remarkable effect.

Claims 1-4 and 7-19

The subject matters of claims 1-4 and 7-19 do not appear to involve an inventive step in view of documents 1-3 cited in the ISR.

Document 3 describes a cleavage site of human VWF.

Therefore, it is not considered especially difficult to use the various fragments containing a cleavage site of human VWF described in documents 1 and 2 for measuring the activity of ADAMTS13.

Furthermore, employing the constitution of the subject matters of claims 1-4 and 7-19 is not considered to exhibit any especially remarkable effect.

Claims 5 and 6

The subject matters of claims 5 and 6 appear to be novel and to involve an inventive step in view of the documents cited in the ISR.

The specific human VWF fragments described in claims 5 and 6 and the said specific fragments being especially excellent as substrates of ADAMTS13 are neither described in any of the documents nor obvious to a person skilled in the art.